Legal Requirements for Patient Registries

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Agenda

- When is the creation of a patient registry (or access to a patient registry) "human subject research" that requires IRB review?
- What should be included in an informed consent document for participation in a patient registry used for clinical research?
- How should a patient registry used for clinical research comply with the HIPAA Privacy Rule and other privacy requirements?
- Who "owns" the data in a patient registry? Is data "ownership" the right question?

Our Hypothetical .....

- Dr. Hart is an interventional cardiologist at the University of Nowhere. He has asked his staff to collect patient information in order to study the success rates of various stents that he utilizes. Dr. Hart's analysis has revealed some surprising findings that he would like to present at the annual meeting of the American College of Cardiology.

Hypo continued....

- Dr. Hart would also like to combine his data with other cardiologists' data to create a registry of patients who have received cardiac stents, in order to contact those patients regarding their interest in participating in future clinical trials. His university department will house and manage the registry.
- Dr. Hart is planning to leave the University and join the University of Somewhere and wants to bring the patient registry with him to his new university.

Human Subject Research

Research

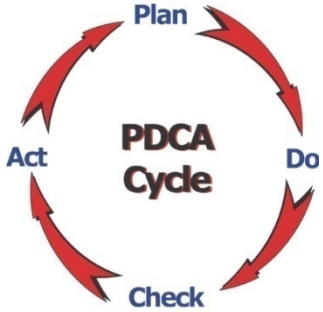
- Common Rule (45 CFR part 46, subpart A)
  - Regulates federally supported "human subjects research"
  - Many institutions have adopted its provisions for non-federally supported research
  - Applies to a project only if:
    - The project is "research"
    - It involves "human subjects"
    - The institution is "engaged" in research
  - Some activities are "research" but do not involve "human subjects" as defined in the Common Rule ... in other cases, an institution supporting human subjects research in some way may not be "engaged" in the research

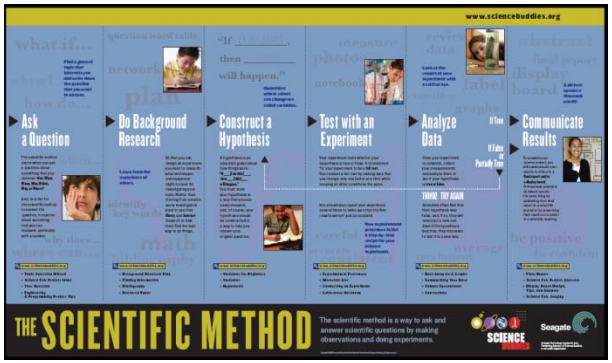
Definitions

- Research is a systematic investigation designed to develop or contribute to generalizable knowledge
- A human subject is a living individual about whom an investigator conducting research obtains data through interaction (e.g., survey) or intervention (e.g., venipuncture or experimental treatment) with the individual, or identifiable private information
- An investigator is someone who is involved in the design, analysis or publication of results. OHRP does not necessarily consider the act of furnishing identifiable or coded private information or specimens to an investigator to, in and of itself, constitute research.
- Obtaining means receiving or accessing identifiable private information or identifiable specimens for research (includes analysis of data or specimens already in the investigator's possession).

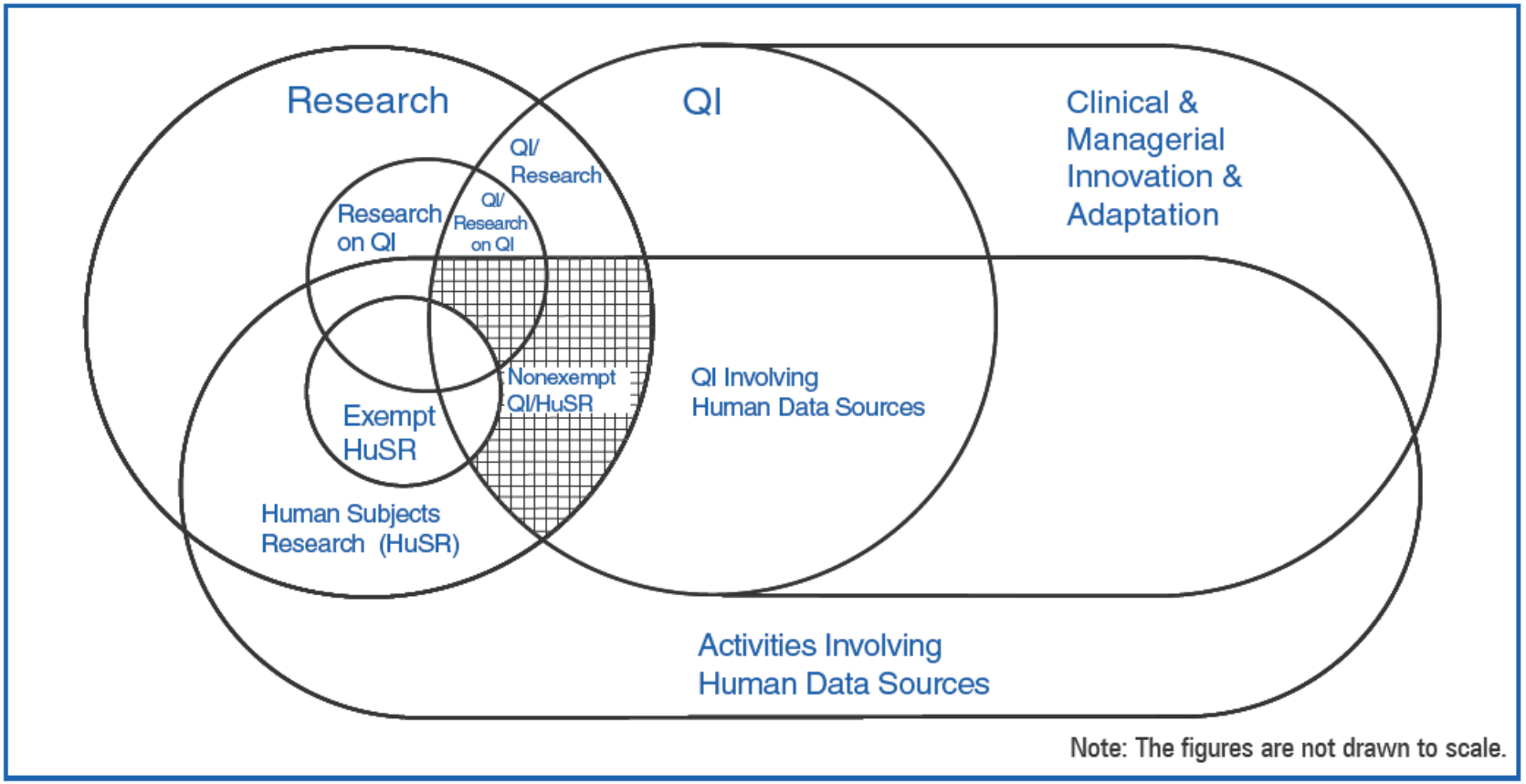
Q.1: Is it Research?

- "Systematic investigation" … "generalizable knowledge"
- The QI/Research conundrum
  - Good QI is conducted systematically
  - Those engaged in QI often want to publish and share positive or unexpected results (and even negative results in some cases)
  - HIPAA adopted a "primary purpose" test but no such test exists under the Common Rule





Put another way …



From: Hastings Center Special Report: Ethics of Using QI Methods to Improve Health Care Quality and Safety (July/August 2006)

QI vs. Research
Hastings Center Rept. 7/2006

1. Are patients ***randomized*** into different intervention groups in order to enhance confidence in differences that might be obscured by nonrandom selection? *Randomization done to achieve equitable allocation of a scarce resource need not be considered and would not result in a "yes" here.*
2. Does the project seek to test issues that are ***beyond current science and experience***, such as new treatments (*i.e.*, is there much controversy about whether the intervention will be beneficial to actual patients – or is it designed simply to move existing evidence into practice?). *If the project is performed to implement existing knowledge to improve care – rather than to develop new knowledge – answer "no".*
3. Are researchers who have no ***ongoing commitment to improvement of the local care situation*** (and who may well have conflicts of interest with the patients involved) involved in key project roles? *Generally answer "yes" even if others on the team do have professional commitments. However, where the project leaders with no clinical commitment are unaffiliated with the project site, it may be that the project site is not engaged – and does not require IRB approval/oversight – even if the project leaders' roles do require IRB oversight at their institutions.*

Hastings Center Rept. (con't)

4. Is the protocol ***fixed*** with a fixed goal, methodology, population, and time period? *If frequent adjustments are made in the intervention, the measurement, and even the goal over time as experience accumulates, the answer is more likely "no."*
5. Will there be ***delayed or ineffective feedback*** of data from monitoring the implementation of changes? *Answer "yes" especially if feedback is delayed or altered in order to avoid biasing the interpretation of data.*
6. Is the project ***funded by an outside organization*** with a commercial interest in the use of the results? Is the sponsor a manufacturer with an interest in the outcome of the project relevant to its products? Is it a non-profit foundation that typically funds research, or internal research accounts? *If the project is funded by third-party payors through clinical reimbursement incentives, or through internal clinical/operations funds vs. research funds, the answer to this question is more likely to be "no."*

Q.2: Does it Involve Human Subjects?

- No if:
  - Data to be shared relate solely to deceased individuals (individuals must be living to be considered human subjects")
  - Data to be shared are completely deidentified (within the meaning of the Common Rule) before the start of the study and consent forms (or IRB-approved waiver) under which data originally were collected did not specifically restrict or limit use of de-identified data for the current project or future research generally

Q.3: Is the Data Provider "Engaged" in Research ?

- **12/2006 DRAFT Revised OHRP Engagement Guidance**
  - Unless it receives a direct HHS award for conducting the research (even if all of the research activities are subcontracted out) a data provider institution is not "engaged" in research if:
    - The data to be disclosed or transferred (which may be identifiable) originally were collected for purposes other than the current project (e.g., clinical care or an unrelated research study); and
    - If the data originally were collected as part of another research project, disclosure is not inconsistent with the research consents (or IRB-approved waiver) under which data originally were collected
  - Note: The recipient institution is engaged in the research, at least if it receives identifiable data, and accordingly must secure IRB approval and consent (or waiver) before proceeding with the study

Q.3: Is the Data Provider Engaged in Research?

- **8/2004 Coded Guidance**
  - The act of providing coded data to a researcher does not make a person an "investigator"
  - Activities that do include: study, interpretation, or analysis of data resulting from coded data or specimens; and authorship of presentations or manuscripts related to the research
  - Note: Obtaining identifiable data or specimens for research purposes is human subjects research

Q.3: Is the Data Provider Engaged in Research?

- **8/2004 Coded Guidance (con't)**
  - Conversely, a project is not considered human subjects research if:
    - Data were not specifically collected for purposes of the current project through an interaction or intervention with living individuals; and
    - Data are coded so that investigators performing the research can't readily ascertain the identity of the affected individuals because, e.g.:
      - Key is destroyed before the research begins
      - Contractual terms agreed to by the recipients prohibit reidentification
      - Existing institutional or IRB policies prohibit release of keys
      - Etc.

Q.4: Are There Other Ways to Reduce Regulatory Burden?

- Exempt research
- Master/umbrella protocols
- Expedited review procedures
- Waiver of informed consent
- Alternatives to multi-institutional approval

Reducing Barriers to Data Sharing

- **Research is "exempt" from IRB oversight under the Common Rule if:**
  - The data to be used already existed at the time the study started; and
  - The data to be used are not directly or indirectly linked to individual subjects; and
  - The IRB or other designated institutional office/official has approved the exemption

- **No new IRB approval or informed consent (or waiver) is required if:**
  - The project is proceeding under a "master" or "umbrella" protocol that covers a broad range of activities or multiple sub-studies
  - The project is performed consistent with that protocol

Reducing Barriers to Data Sharing

- **Expedited review procedures**
  - Many registry-based projects may be eligible for expedited review
  - Project must be minimal risk and fall into one of several pre-defined categories, including:
    - Collection of certain tissues and other products by non-invasive or minimally invasive means
    - Secondary use

- **Waiver of informed consent**

Reducing Barriers to Data Sharing

- **Consider alternatives to multi-institutional review and approval:**
  - CIRB
  - Commercial IRB
  - Defer or accept under an IRB Authorization Agreement

Special Challenges

- **Secondary research inconsistent with original consent**
  - Some IRBs will bar reuse altogether
  - Some will require new IRB exemption
  - Some will require new IRB approval and consent or waiver
- **Consent withdrawn**
  - Meaning of term is controversial
  - May require de-identification, destruction, or even return

Questions for IRBs (Summary)

- Is the project research?
  - Systematic investigation
  - Generalizable knowledge
- Does it involve human subjects?
  - Living or deceased
  - Investigator performing research obtains
    - Data through interaction or intervention
    - Identifiable private information
- Is this institution engaged?

Informed Consent

Informed Consent Issues

- Regulations require informed consent to include:
  - Explanation of purposes of the research;
  - Description of the procedures to be followed.
- 45 C.F.R. 46.116(a)(1).

OHRP Guidance on Use of Stored Data or Tissues (1996)

- Should include clear description of:
  - Operation of repository;
  - Specific types of research to be conducted;
  - Conditions under which data will be released; and
  - Procedures for protecting subjects' privacy and confidentiality of data.

OHRP Guidance on Use of Stored Data or Tissues (1996)

- Informed consent information describing the nature and purposes of the research should be as specific as possible.
- Where human genetic research is anticipated, informed consent information should include information about the consequences of DNA typing.

SACHRP Recommendations (2005)

- If future uses are unclear at the time of collection:
  - The future uses are new protocols (requiring new IRB submissions); and
  - The IRB may either require new informed consent or grant a waiver of informed consent for the new uses.

Practical Guidance

- If a specific use of data is described in the initial collection protocol, describe that in initial consent. Consent should be sufficient.
  - Description should be specific

Practical Guidance
"Future Unspecified Research"

- For other uses that are not clearly described in the initial protocol, describe the general types of research that might be done.
  - "Future research about the causes of cancer...."

Practical Guidance "Future Unspecified Research"

- When a proposal is made to conduct future research, submit IRB application.
- IRB will consider if research is of the general type described in initial consent.
  - Yes: approve/waive consent.
  - No: disapprove or require consent.

Protecting Privacy

HIPAA Compliance

- The HIPAA research rules apply when a HIPAA "covered entity" internally accesses or externally discloses protected health information (PHI) of a patient or a patient's family members, household members, or employers
- PHI includes any information containing HIPAA "identifiers" (see next slide)

HIPAA "Identifiers"

- Name;
- Street address, city, county, precinct, or zip code (unless only the first three digits of the zip code are used and the area has more than 20,000 residents);
- **The month and day of dates directly related to an individual, such as birth date, admission date, discharge date, dates of service, or date of death**;
- Age if over 89 (unless aggregated into a single category of age 90 and older);
- Telephone numbers;
- Fax numbers;
- Email addresses;
- Social security numbers;
- Medical record numbers;
- Health plan beneficiary numbers;
- Account numbers;
- Certificate/license numbers;
- Vehicle identifiers, serial numbers, and license plate numbers;
- Device identifiers and serial numbers;
- Web Universal Resource Locators (URLs) and Internet Protocol (IP) addresses;
- Biometric identifiers, such as fingerprints
- Full-face photographs and any comparable images; or
- Any other unique identifying number, characteristic, or code.

HIPAA Compliance Routes

- Okay if meet one of nine possible HIPAA compliance options (see White Paper)
- We will cover:
  - De-identifying information
  - Using a "Limited Data Set"
  - Identifying potential registry participants
  - Contacting registry participants to participate in clinical trials
  - Seeking HIPAA authorization

When Is Data De-identified?

- HIPAA de-identification
  - Remove or code HIPAA identifiers (but code cannot be derived from patient identifiers); or
  - Document that there is a statistically "very small" risk that information could be used to identify patient.
  - Different than Common Rule: de-identified if investigator cannot reasonably determine identity.

Coding Data

- Common Rule: Investigator cannot reasonably determine identity if:
  - Destroy key to code before research begins;
  - Investigators and holder of key enter into agreement prohibiting release of key to investigators until individuals are deceased;
  - Have IRB approve written policies and procedures for a repository or data management center that prohibit the release of the key to investigators until individuals deceased; or
  - Determine that other legal requirements exist that prohibit release of key to investigators
- Compare HIPAA: code cannot be derived from HIPAA identifiers

Using a Limited Data Set

- May use a Limited Data Set for research, health care operations (including QI) and public health purposes
- Partially de-identified data; may include:":
  - Geographic designations above street level or PO Box
  - Dates related to the individual
  - Any other unique identifying number, characteristic or code that is not expressly listed as a HIPAA identifier
- Need a "Data Use Agreement" in place with both internal and external researchers

Identifying Potential Registry Participants

- HIPAA "preparatory to research" activities
  - Requires representation from researcher that:
    - PHI is sought solely to prepare for research;
    - PHI is necessary to prepare for research; and
    - No information identifying individuals will be removed from the premises in the course of the review
- Remote access only if obtain representation that researcher will not print, copy, save, or electronically fax PHI
  - Reliance on researcher must be "reasonable"– must have way of managing compliance
  - Must comply with the HIPAA Security Rule (standards for access control, integrity, transmission security)

Identifying Potential Registry Participants

- IRB waiver of HIPAA authorization
  - 1. The use or disclosure of the subjects' identifiable information involves no more than minimal risk to their privacy;
  - 2. The research could not practicably be conducted without the waiver or alteration of authorization; and
  - 3. The research could not practicably be conducted without access to and use of information identifying the subjects
- Common Rule requires IRB waiver of informed consent to review records of living patients and to identify potential research subjects

Recruiting Registry Participants for Clinical Trials

- Provider may contact own patients
  - "Treatment" if discuss treatment alternatives or "health care operations" to seek authorization to participate in clinical trial
- Provider may have third person contact provider's patients (with HIPAA business associate contract in place)
  - "Health care operations" to seek authorization
- Researcher may request IRB to partially waive HIPAA authorization
- Does not fall within the "preparatory to research" HIPAA exception

HIPAA Authorization Problems

- Cannot combine HIPAA authorization with informed consent to store PHI for future research
  - HIPAA authorization may not seek permission to use or disclose PHI for future unspecified research, because HHS has concluded that authorization must be protocol-specific or must be for storage only
  - Options:
    - Have separate informed consent and HIPAA authorization forms; or
    - Have separate sections of form separately signed.

Authorization Problems

- Cannot combine authorizations to store PHI in a repository and to use PHI for a clinical trial
  - May require participant to sign authorization to use or disclose PHI for clinical trial, as condition of participating in a clinical trial
  - Cannot require participant to sign authorization to collect PHI for storage in repository (if PHI will be used beyond the particular clinical trial)
  - Cannot combine these authorizations (into a "compound authorization") where subject receiving treatment in a clinical trial
  - Options:
    - Have separate authorization forms for particular clinical trial and collection of PHI for repository; or
    - Make clear that participant does not have to agree to portion that authorizes collection of PHI for repository

Involvement of Non-HIPAA Covered Entities: Protection after Disclosure of PHI

- HIPAA Privacy Rule does not prohibit use for secondary research by non-covered entities: authorization informs subjects that once disclosed, PHI may not be protected by HIPAA
- Secondary research must comply with scope of the informed consent document
  - IRB must determine that there are adequate provisions to protect the privacy of subjects and to maintain data confidentiality (45 CFR 46.111)

Certificates of Confidentiality

- Certificates of Confidentiality available from NIH for "sensitive" research information where disclosure of identifying information could damage subjects' financial standing, employability, insurability or reputation
  - Research collecting information related to genetics, psychological well being, sexual behavior, drug use, criminal activities
  - Research where subjects may be involved in litigation related to exposures under study
  - See Certificates of Confidentiality Kiosk: http://grants.nih.gov/grants/policy/coc/

Stewardship/Ownership

Stewardship/Ownership and Other Issues

- Do researchers "own" the data in their registries?
  - Clinical information is in medical record: HIPAA gives patients some, but not total, right to control how their medical record information is used.
  - Physician/clinic still retains right to use, subject to applicable restrictions.

Stewardship/Ownership and Other Issues

- What about in research context?
  - Data – National Committee on Vital and Health Statistics (NCVHS) 2007 report speaks of data "stewardship."
  - "Steward" – one who assumes responsibility for another person's property.

Stewardship/Ownership and Other Issues

- NCVHS Report: Stewardship responsibilities include HIPAA obligations for covered entities, and compliance with OHRP & FDA rules, where applicable.
- NCVHS proposes comprehensive and consistent guidelines for all users.

Stewardship/Ownership and Other Issues

- Biological specimens:
  - Washington University vs. Catalona – federal court held that research institution "owns" samples that were given by subjects as "gifts."
    - Possibility for state-by-state variation?
  - NCI Best Practices for Biospecimen Resources - research institution is "custodian" of samples for subject.

Stewardship/Ownership and Other Issues

- Regardless of ownership vs. stewardship or custodianship:
  - Data & specimens should be used only in accordance with informed consent provided by subject.

Stewardship/Ownership and Other Issues

- What about subject's right to "withdraw" from research?
  - Catalona court indicated that researchers could choose between discarding or de-identifying remaining specimens.
  - Subjects do not have right to get samples back, or force researcher to give them to someone else.

Stewardship/Ownership and Other Issues

- What about subject's right to "withdraw" from research?
  - NCI Best Practices generally agree with discarding or de-identification options from Catalona.
  - However, report also suggests possible need to return specimens based on cultural concerns.

Questions?